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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,143	01/16/2001	Muraleedharan G. Nair	MSU 4.1-541	4327

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EXAMINER	
LEITH, PATRICIA A	
ART UNIT	PAPER NUMBER
1655	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/761,143	NAIR ET AL.	
	Examiner	Art Unit	
	Patricia Leith	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,15-18,27-30 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,15-18,27-30 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-6, 15-18, 27-30 and 34 are pending in the application and were examined on their merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a previous Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-6, 15-18, 27-30 and 34 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. It does not appear that Applicants' original disclosure discussed lyophilization of an anthocyanin and an

isolated cyanidin. Therefore, 'lyophilized' as it is used in the claim to describe an isolated cyanidin and an anthocyanin is considered New Matter.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,818,234, in view of Gryglewski et al. (1987) in view of Hellburg et al. (US 5,691,360 A).

Claims 1-15 of '234 teach a method for alleviating or reducing pain an a mammal by administration of anthocyanins. Although the claims do not specifically state wherein

cyclooxygenase is inhibited, this is the only necessary conclusion based upon the teachings of the '234 specification. It is drawn from the claims of '234 that the anthocyanins are extracted from the other endogenous ingredients of the cherry and therefore it is deemed that the extract does not contain natural acids. The claims of '234 do not specifically teach the incorporation of isolated cyanidin or a food-grade acid.

Gryglewski et al. (1987) studied the anti-inflammatory mechanism of 3-cyanidol (cyanidin) *inter alia* and discovered that cyanidin inhibits cyclooxygenase (see entire reference, especially pp. 318 – 319 and Table 10). It is noted that cyclooxygenase is a synonym for prostaglandin H synthase/synthetase.

Hellburg et al. (US 5,691,360 A) taught that:

> The antioxidant activity of the phenolic compounds is enhanced by stabilizing the phenoxyl flee radical or by facilitating the transfer of the free radical to other components of the detoxification mechanism, such as GSH or vitamin C. Alkyl substituents stabilize the phenoxyl free radical by electron donation and the stearic bulk of ortho substituents reduces the propensity of the phenoxyl radical to participate in free radical chain reactions (col. 6, line 66-col.7, line 6).

One of ordinary skill in the art would have been motivated to add a food grade acid such as vitamin c (ascorbic acid) to a combination of anthocyanin and cyanidin in order to stabilize the antioxidant activities of anthocyanin and cyanidin. One of ordinary skill in the art would have had a reasonable expectation that vitamin c, being a strong antioxidant and also being know to stabilize phenolic compounds, would have been

advantageous to add to a composition comprising the phenolics anthocyanin and cyanidin.

Therefore, it would have been obvious to administer cyanidin along with anthocyanins a cyanidin-3-glucoside which yield the aglycone structures of cyanidin because it was already known in the art that cyanidin inhibited cyclooxygenase and was therefore an inhibitor of inflammation. One of ordinary skill in the art would have had a reasonable expectation that the combination of cyanidin and anthocyanin would have provided for a combined effect of treating inflammation.

Claims 1-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,194,469 , in view of Gryglewski et al. (1987) in view of Hellburg et al. (US 5,691,360 A).

Claims 1-8 of '469 teach a method for inhibiting cyclooxygenase or prostaglandin H synthase via administration of specific anthocyanins from a cherry. It is drawn from the claims that the anthocyanins are extracted from the other endogenous ingredients of the cherry and therefore it is deemed that the extract does not contain natural acids. The claims do not specifically teach the incorporation of isolated cyanidin or a food-grade acid.

Gryglewski et al. (1987) studied the anti-inflammatory mechanism of 3-cyanidol (cyanidin) *inter alia* and discovered that cyanidin inhibits cyclooxygenase (see entire reference, especially pp. 318 – 319 and Table 10). It is noted that cyclooxygenase is a synonym for prostaglandin H synthase/synthetase.

Hellburg et al. (US 5,691,360 A) taught that:

> The antioxidant activity of the phenolic compounds is enhanced by stabilizing the phenoxyl flee radical or by facilitating the transfer of the free radical to other components of the detoxification mechanism, such as GSH or vitamin C. Alkyl substituents stabilize the phenoxyl free radical by electron donation and the stearic bulk of ortho substituents reduces the propensity of the phenoxyl radical to participate in free radical chain reactions (col. 6, line 66-col.7, line 6).

One of ordinary skill in the art would have been motivated to add a food grade acid such as vitamin c (ascorbic acid) to a combination of anthocyanin and cyanidin in order to stabilize the antioxidant activities of anthocyanin and cyanidin. One of ordinary skill in the art would have had a reasonable expectation that vitamin c, being a strong antioxidant and also being know to stabilize phenolic compounds, would have been advantageous to add to a composition comprising the phenolics anthocyanin and cyanidin.

Therefore, it would have been obvious to administer cyanidin along with anthocyanins a cyanidin-3-glucoside which yield the aglycone structures of cyanidin because it was already known in the art that cyanidin inhibited cyclooxygenase and was

therefore an inhibitor of inflammation. One of ordinary skill in the art would have had a reasonable expectation that the combination of cyanidin and anthocyanin would have provided for a combined effect of treating inflammation.

Claims 1-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,676,978 in view of Gryglewski et al. (1987) in view of Hellburg et al. (US 5,691,360 A).

Claims 1-8 of '978 teach a method for inhibiting inflammation via administration of specific anthocyanins from a cherry. Although the claims do not specifically state wherein cyclooxygenase is inhibited, this is the only necessary conclusion based upon the teachings of the '978 specification. The claims specifically state that the extract is free of organic acids from the cherry. The claims do not specifically teach the incorporation of isolated cyanidin or a food-grade acid.

Gryglewski et al. (1987) studied the anti-inflammatory mechanism of 3-cyanidol (cyanidin) *inter alia* and discovered that cyanidin inhibits cyclooxygenase (see entire reference, especially pp. 318 – 319 and Table 10). It is noted that cyclooxygenase is a synonym for prostaglandin H synthase/synthetase.

Hellburg et al. (US 5,691,360 A) taught that:

> The antioxidant activity of the phenolic compounds is enhanced by stabilizing the phenoxyl flee radical or by facilitating the transfer of the

> free radical to other components of the detoxification mechanism, such as GSH or vitamin C. Alkyl substituents stabilize the phenoxyl free radical by electron donation and the stearic bulk of ortho substituents reduces the propensity of the phenoxyl radical to participate in free radical chain reactions (col. 6, line 66-col.7, line 6).

One of ordinary skill in the art would have been motivated to add a food grade acid such as vitamin c (ascorbic acid) to a combination of anthocyanin and cyanidin in order to stabilize the antioxidant activities of anthocyanin and cyanidin. One of ordinary skill in the art would have had a reasonable expectation that vitamin c, being a strong antioxidant and also being know to stabilize phenolic compounds, would have been advantageous to add to a composition comprising the phenolics anthocyanin and cyanidin.

Therefore, it would have been obvious to administer cyanidin along with anthocyanins a cyanidin-3-glucoside which yield the aglycone structures of cyanidin because it was already known in the art that cyanidin inhibited cyclooxygenase and was therefore an inhibitor of inflammation. One of ordinary skill in the art would have had a reasonable expectation that the combination of cyanidin and anthocyanin would have provided for a combined effect of treating inflammation.

It is noted that the Office is aware that three (3) Terminal Disclaimers were filed on 8/24/07. However, these Terminal Disclaimers have not been reviewed and therefore the rejections remain pending.

Claim Rejections - 35 USC § 103

Claims 1, 3-6, 15-18, 27-30 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gryglewski et al. (1987) in view of Lietti et al. (GB 1,589,294). in view of Hellburg et al. (US 5,691,360 A) in view of Brenner (US 5,462,932 A) in view of Roy (US 4,712,310 A).

The teachings of Gryglewski et al., Lietti et al, Hellberg et al. and Brenner were keenly discussed in the previous Office Action. These references did not teach lyophilization.

Drugs are routinely lyophilized in order to incorporate into tablets as per Roy (US 4,712,310 A) (see entire reference, especially col. 3, lines 22-68).

One of ordinary skill in the art would have been motivated to either 1) lyophilize a mixture of isolated cyanidin and an anthocyanin because this would have been a routine means for tableting the pharmaceutical preparation or 2) lyophilized the wild cherry as disclosed by Brenner in order to create a wild cherry powder.

Applicant's arguments were fully considered, but were not found persuasive.

Applicant argues that:

> There is no way that conclusions in relation to Compounds I or II of the Hellberg et al. patent could be used by one skilled in the art to deduce anything about the claimed invention. This is nothing more than an attempted hindsight reconstruction of the claimed invention from Applicants' own disclosure and is not supported by the facts. The Nair declaration Under 37 CFR 1.132 filed in this application clearly shows that the problem is the loss of the anthocyanins to hydrolysis. This has nothing to do with the compounds of Hellberg et al. the combination rejection clearly is incorrect (p. 8, Remarks).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Taken as a whole, it would have been obvious to one of ordinary skill in the art to produce the claimed invention.

To reiterate from Hellburg et al.:

> The antioxidant activity of the phenolic compounds is enhanced by stabilizing the phenoxyl flee radical **or by facilitating the transfer of the free radical to other components of the detoxification mechanism, such as GSH** or vitamin C...

While Hellburg et al. does not specifically disclose the structures of anthocyanins, or cyanidin, Hellberg et al. clearly teaches that antioxidant phenolics are stabilized by Vitamin C because phenolic antioxidants in the presence of Vitamin C can transfer free radicals to the Vitamin C in order to continue the antioxidant process. Cyanidin, or 'cyanidol-3' as referred to by Gryglewski et al. were clearly phenolic antioxidant compounds (see entire reference, and more specifically, see p. 321, column 1, second full paragraph). Thus, the ordinary artisan clearly would have seen the advantage of the addition of an antioxidant compound such as Vitamin C into a composition containing antioxidant phenolics

Applicant argues:

Lietti et al. does not support the combination rejection. the reference teaches only cyanidin as a useful product and hydrolyzes the anthocyanins to obtain the cyanidin. Nothing suggests the claimed compositions, since Lietti et al. would hydrolyze them away before use, thus 'teaching away' from the claimed invention (paragraph bridging pages 8-9)

However, to reiterate from the Office Action of 12/15/06:

Thus, *in-vivo*, anthocyanins are converted (hydrolyzed) to the non-glycosylated anthocyanidins before entry into the intestinal tract. Consequently, one of ordinary skill in the art would have recognized that cyanidin and the glycosidic forms of cyanidin, would have been virtual pharmaceutical equivalents since anthocyanins essentially degrade in the body to cyanidin (p. 7, Office Action).

Lietti et al. clearly teach that warming of anthocyanins in the presence of an acid produces anthocyanidins. The ordinary artisan would have easily concluded therefore, that anthocyanins are hydrolyzed in the digestive tract to anthocyanidins. Thus, the ordinary artisan would have recognized that the effects of oral ingestion of anthocyanins and anthocyanidins would have been pharmaceutically equivalent.

Applicant argues that "Gryglewski et al. does not show any particular activity for cyanidol (cyanidin)" (p. 9, Remarks). However, this argument is without merit because it is clear on the record that Gryglewski et al. demonstrated the anti-oxidant and cyclooxygenase inhibition effects of cyanidol (cyanidin).

It is also pointed out that wild cherry powder necessarily contains anthocyanins. As stated in this, and the previous Office Action, it would have been obvious to add cyanidin (isolated) to a wild cherry powder to produce a flavorful orally-ingestible composition for inhibiting cyclooxygenase. It further would have been obvious to add a food grade acid such as ascorbic acid (vitamin C) because, as stated *supra*, Vitamin C is a well-known antioxidant, and Vitamin C is known to stabilize phenolic antioxidants.

The Supreme court has acknowledged that:

> When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. **If a person of ordinary skill can implement a predictable varition..103 likely bars its patentability**...if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person's

> skill. A court must ask whether the improvement is more than the predictable use of prior-art elements according to their established functions...
>
> ...**the combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results** (see *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 U.S. 2007) emphasis added.

[If]... there are [a] finite number of identified, predictable solutions, [a] person of ordinary skill in art has good reason to pursue known options within his or her technical grasp, and if this leads to anticipated success, it is likely product of ordinary skill and common sense, not innovation *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 U.S. 2007.From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia Leith whose telephone number is (571) 272-0968. The examiner can normally be reached on Monday - Friday 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Patricia Leith
Primary Examiner
Art Unit 1655

October 25, 2007